REMARKS

Claims 1, 2, 4-7, 10, 17 and 26 are all the claims pending in the application.

A substitute Sequence Listing is being filed simultaneously herewith. Such has been amended in order to correct obvious typographical errors therein. Support for the amendment of SEQ ID NO:3 and SEQ ID NO:4 can be found, *inter alia*, in the nucleotide sequence of GenBank No. AI170665. Further, support for GenBank No. AI170665 can be found, *inter alia*, in Example 3 of the present specification. Hence, the correction of the Sequence Listing does not constitute new matter, and thus entry is respectfully requested.

I. Claims 1, 2, 4-7, 10, 17 and 26 are Patentable under 35 U.S.C. § 101 and 35 U.S.C. § 112, First Paragraph

At page 2 of the Office Action, the office rejects Claims 1, 2, 4-7, 10, 17 and 26 because the Examiner alleges that the specification does not disclose the statistical significance of the data described in Example 4 and Figures 1 and 2; the specification fails to present any scientific reasoning as how this data support the role of C1 protein in Alzheimer's disease; the statement that C1 has "an inhibitory activity" appears to be not fully supported by the evidence presented by Applicants because no control data regarding spontaneous secretion of Aβ from the wild-type cells; the specification fails to explain how spontaneous secretion of Aβ in cells transfected with C1 relates to etiology of Alzheimer's disease and the Examiner fails to find a specific connection between the cited art and the instant currently claimed polypeptide C1 of SEQ ID NO:1.

Applicants' respectfully disagree. The relation between cell death and β-amyloid secretion disclosed in the Example and neurodegenerative diseases such as Alzheimer's disease is taught in the BACKGROUND ART section of the present specification. Specifically, it is taught that (A) if a Pael receptor has abnormality (such as an incomplete higher-order structure), it is usually rapidly decomposed by the action of Parkin, but when the proteolysis system is suppressed, abnormal Pael receptors are accumulated in endoplasmic reticula, and the cell falls into cell-death due to endoplasmic reticulum stress (*Cell*, 105:891-902 (2001)); and (B) production of β-amyloid is increased due to lack of Ire1 participating in endoplasmic reticulum stress response (*Biochem. Biophys. Acta.*, 1536:85-96 (2001); and *J. Biol. Chem.*, 276:2108-2114 (2001)) (see page 1, line 25 to page 2, line 4).

The expression of C1 gene is induced by the endoplasmic reticulum stress, and thus it is suggested that the induction of the expression of C1 gene causes induction of cell death. As explained above, it has been reported that in Alzheimer's disease, Parkinson's disease and the like, the endoplasmic reticulum stress response is induced, and the endoplasmic reticulum stress causes functional disorder.

It is also known to one of ordinary skill that the endoplasmic reticulum stress is induced by accumulation of abnormal proteins in cells. Since one of the characteristic lesions common to neurodegenerative diseases is the accumulation of abnormal proteins, it is expected that the endoplasmic reticulum stress is induced in neurodegenerative diseases. For this reason, expression of C1 gene is also believed to be induced in neurodegenerative diseases and is related to phenomena such as cell death.

Those skilled in the art would understand from the specification, as taught above, and by Examples 4 and 5, that inhibition of the expression of C1 results in inhibition of cell death and an increase in the secretion of β-amyloids, and thus it would be effective for treating Alzheimer's disease, Parkinson's disease and the like. Thus, it would be reasonable that compounds that inhibit the expression (or the activity) of C1 can be used for treating neurodegenerative disease such as Alzheimer's disease.

Accordingly, the present invention has a specific and substantial credible utility of screening for compounds that inhibit the activity of the protein of the present invention. The present invention has the specific and substantial credible utility of screening for compounds that inhibit the expression of the protein. Thus, the inventions of Claims 1, 2, 4-7 and 17 have a specific and substantial credible utility. Therefore, the rejection should be withdrawn.

As for Claims 1, 2, 10 and 26, in neurodegenerative diseases such as Alzheimer's disease or Parkinson's disease, endoplasmic reticulum stress response is induced and the expression level of C1 is expected to be enhanced. Therefore, the claimed product can be used as an antigen in the immunological treatment of such diseases. The utility of the claimed invention is limited to the immunological treatment. At present, the use of C1 as an antigen in an immunological treatment of the disease is one of possible utilities of C1.

Regarding the statistical significance of the data shown in Examples 4 and 5 of the present application, in the experiment taught in Example 4, DNA cleavage was promoted in the

cells transformed with the C1 gene, as compared with the SK-N-AS cells transformed with pcDNA3.1 (control cells) (*see also* Figs. 1 and 2). Although the Examiner states that there is only a slight increase as compared to control cells, those skilled in the art would understand that this increase is statistically significant. Applicants have determined that when the DP5 gene, well-known to induce cell death (*J. Biol. Chem.*, 274:7975 (1999)), was verified by the same verification method as that used in Example 4, the change in the amount, in terms of OD405-492, of cleaved DNA in a cell is almost the same level as that shown in Example 4.

In an experiment of gene transfer such as Example 5, it is a common practice that a vector which was used for transduction of the gene of interest, or a LacZ vector, or a GFP expression vector is used for verification of the experiment as a control in order to avoid any effect from the employed gene transduction process. In the experiment taught in Example 5, no data is shown for comparison between the cell used for the gene transfer and the wild-type cell, which is in conformity to the common practice explained above. Applicants have determined that there was no difference in Aβ secretion was observed between the case where cells to which a vector without a gene for expression had been introduced were used and the case where cells to which a GFP expression vector had been introduced were used.

Thus, one of ordinary skill in the art concludes from the results shown in Example 5, in which an inhibitory activity of C1 against Aβ secretion as compared to GFP as a control is presented, in view of the common technical general knowledge, that C1 has the inhibitory activity against the Aβ secretion.

Withdrawal of the rejection is therefore kindly requested.

II. Clarification of Applicants' Remarks of August 13, 2007

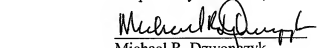
At page 7 of the Amendment under 37 C.F.R. § 1.111, Applicants stated, "thus, those skilled in the art would understand that an agent that promotes cell death and inhibits secretion of amyloid β-proteins can be used for treatment of neurodegenerative diseases such as Alzheimer's disease." Applicants desire to clarity this statement As explained above, C1 promotes cell death and inhibits secretion of amyloid β-protein. In neurodegenerative diseases such as Alzheimer's disease or Parkinson's disease, endoplasmic reticulum stress response is induced and the expression level of C1 is expected to be enhanced. Therefore, C1 can rather be used as, for

example, an antigen in the immunological treatment of such diseases. Applicants kindly thank the Office for acknowledging clarification of this point.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



Michael R. Dzwonczyk
Registration No. 36,787

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860
WASHINGTON OFFICE
23373
CUSTOMER NUMBER

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